

**AMENDMENTS TO THE CLAIMS**

This listing of claims will replace all prior versions, and listings, of claims in the application:

1. (Original) A method for identifying a ligand of a target macromolecule comprising the steps of:

- a) soaking one or more crystals of the target macromolecule in a solution containing a collection of compounds generated in situ or separate from the crystal, where the solution has been prepared without the purification of the synthesized collection of compounds;
- b) obtaining an X-ray crystal diffraction pattern of the soaked macromolecule crystal; and
- c) using said X-ray crystal diffraction pattern to identify any compound bound to the macromolecule crystal, said compound being a ligand of the target macromolecule.

2. (Original) A method for identifying a ligand of a target macromolecule comprising the steps of:

- a) synthesizing a collection of compounds, which are suitable for screening against a target macromolecule, in a solution containing one or more crystals of the target macromolecule;
- b) obtaining an X-ray crystal diffraction pattern of the soaked macromolecule crystal; and
- c) using said X-ray crystal diffraction pattern to identify any compound bound to

the macromolecule crystal, said compound being a ligand of the target macromolecule.

3. (Original) A method for identifying a ligand of a target macromolecule comprising the steps of:

- a) synthesizing a collection of unpurified compounds, which are suitable for screening against a target macromolecule;
- b) adding the collection of compounds to a solution containing one or more crystals of the target macromolecule;
- c) obtaining an X-ray crystal diffraction pattern of the soaked macromolecule crystal; and
- d) using said X-ray crystal diffraction pattern to identify any compound bound to the macromolecule crystal, said compound being a ligand of the target macromolecule.

4. (Original) A method according to claim 3, wherein if step a) takes place in a solvent which is not compatible with the macromolecule crystals, then the method comprises the further step after step a) of separating the collection of compounds from the solvent in which the compounds were synthesised.

5. (Original) A method according to claim 3, wherein if step a) takes place in a solvent which is not compatible with the macromolecule crystals, the solvent in which

step a) takes place is separated from the solution containing the one or more macromolecule crystals by a permeable membrane.

6. (Currently Amended) A method according to ~~any one of claims~~ claim 1 to 5, wherein the target macromolecule is selected from the group consisting of: proteins, ribose nucleic acids, deoxy ribose nucleic acid, and complexes of combinations of these.

7. (Original) A method according to claim 6, wherein the target macromolecule is a protein.

8. (Currently Amended) A method according to ~~any one of claims~~ claim 1 to 7, wherein the collection of compounds are synthesised individually and then mixed together.

9. (Currently Amended) A method according to ~~any one of claims~~ claim 1 to 7, wherein the collection of compounds are synthesised as a mixture by combinatorial chemistry.

10. (Currently Amended) A method according to ~~any one of claims~~ claim 1 to 9, wherein the members of the collection of compounds are present at a concentration of at least 10 times their  $K_i$ .

11. (Currently Amended) A method according to ~~any one of claims~~claim 1 to 10,  
wherein the amount of each compound being a member of the collection of compounds,  
present in the solution will be present at a concentration which is at least 10 times as  
much as the concentration of the target macromolecule in the reaction system.

12. (Currently Amended) A method according to ~~any one of claims~~claim 1 to 11,  
wherein the members of the collection of compounds do not bind covalently to the target  
macromolecule.